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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/617,846 | 07/10/2003 | Julie A. Johnson | UF-265CXCD1 | 8218 |

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| EXAMINER | |
|---|---|
| FREDMAN, JEFFREY NORMAN | |
| ART UNIT | PAPER NUMBER |
| 1637 | |

DATE MAILED: 01/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/617,846 | JOHNSON, JULIE A. | |
| | Examiner | Art Unit | |
| | Jeffrey Fredman | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maqbool et al (Lancet (1999) 353:897) in view of Mason et al (J. Biol. Chem. (1999) 274:12670-12674) and further in view of Podlowski et al (J. Mol. Med. (2000) 78:87-93).

Maqbool teaches a method of screening for B1 adrenoceptor polymorphisms (see page 897, column 1) comprising:

(a) genotyping the B1 adrenergic receptor of an individual to codon 49 and codon 389 (see page 897, column 1 and figure 1)

Maqbool suggests, but does not teach, that the presence of the polymorphisms are indicative of a likely response to a beta blocker medication (see page 897, column 1).

With regard to claims 3-6, 8-11, Maqbool teaches that the haplotypes are heterozygous and homozygous SER49 or ARG389, but that no one was homozygous for GLY49 (see page 897, column 1).

Maqbool does not teach the specific beta blockers of claims 2 or 7, nor does Maqbool directly predict the effects of the polymorphisms.

Mason teaches a method of screening for B1 adrenoceptor polymorphisms (see page 12670, column 2) comprising:

(a) genotyping the B1 adrenergic receptor of an individual to codon 389 (see page abstract and page 12670, column 2)

Mason suggests that the presence of the polymorphisms are indicative of a likely response to a beta blocker medication (see page 12674, column 1).

In particular, Mason expressly teaches that the presence of the Arg-389 phenotype is predicted to be responsive to beta blocker therapy and consequently

With regard to claims 2, 7, 12, Mason teaches that propranolol is a beta blocker which differentially effects Gly389 and Arg389 (see page 12671, table I).

Podlowski teaches that the Ser49 mutation is associated with idiopathic dilated cardiomyopathy (see page 92, column 1, for example). Podlowski teaches that Ser49 in both homozygous and heterozygous individuals is associated with IDCM (see apge 91, column 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to genotype the polymorphisms and prescribe beta blockers based upon the polymorphism results since Maqbool teaches "Since blockade of this receptor prevents myocardial infarction and prolongs life in patients after myocardial infarction or with chronic heart failure, exploring the effects of these gene variants on response to treatment with B-adrenoreceptor antagonists and on prognosis would be useful (see page 879, column 1)". Further, Mason teaches "Based on our current results, it might be predicted that individuals bearing the Arg-389 receptor would be most responsive to B-blocker therapy because they would have a genetically determined B1AR that achieves a greater stimulation of adenyl cyclase (see page 12674, column 1)". Thus, Mason expressly predicts and teaches the effect of the codon 389 polymorphism and suggests determining the effect of different antagonists on these gene variants, which is an express suggestion that some variants are more likely to respond to the beta blockers (which are B-adrenoreceptor antagonists) than other variants. Podlowski teaches that Ser49 is associated with IDCM (see page 92, column 1).

So an ordinary practitioner, expressly told by Mason that patients with more Arg389 would be more responsive to beta blocker therapy, and expressly told by Podlowski that Ser49 is associated with IDCM and therefore also responsiveness to beta blocker therapy, would have been motivated to genotype for these two polymorphisms in order to prescribe beta blockers to individuals with these alleles, since

individuals with these alleles are predicted to be more responsive to beta blocker therapy by Mason and more in need of therapy by Podlowski.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

1/4/04